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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,461	03/11/2005	John Peter Gilday	056291-5201	5299

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EXAMINER	
ANDERSON, REBECCA L	
ART UNIT	PAPER NUMBER
1626	
MAIL DATE	DELIVERY MODE
11/26/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,461	GILDAY ET AL.	
	Examiner	Art Unit	
	REBECCA L. ANDERSON	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-8 and 30-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-8 and 30-52* is/are rejected.

7)☒ Claim(s) *45 and 51* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 4-8 and 30-52 are currently pending in the instant application. Claims 45 and 51 are objected and claims 1, 4-8 and 30-52 are rejected.

Response to Amendment and Arguments

Applicant's amendment and arguments filed 13 August 2008 have been fully considered and entered into the application.

Applicant's amendment has overcome the objection to the specification and has overcome the 35 USC 112 2nd paragraph rejection of the claims.

In regards to the 35 USC 103(a) rejection, Applicants argue that the Examiner has used impermissible hindsight. This argument is not persuasive as it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicants argue that the claimed process provides significant advantages of reduced time and cost particularly in large scale commercial production. This argument is not persuasive as an Attorney's arguments of unexpected results cannot talke the place of evidence in the record.

Applicants argue that the Examiner's statement that "since each step of the process appears to be relatively complete in itself and there is no indication of an

interaction between steps" is not accurate with respect to the new claims. This argument is not persuasive as the statement by the Examiner is that "since each step of the process appears to be relatively complete in itself and there is no indication of an interaction between steps of such a type that would lead one of ordinary skill in the art to doubt that a substitution of alternative steps known to the art could be made." The Examiner has concluded that there is no indication of an interaction between the steps of such a type that would lead one of ordinary skill in the art to doubt that a substitution of alternative steps known in the art could be made. The examiner has not concluded that there is no interaction between steps, but that there is no interaction that would lead one to doubt that alternative steps could be made.

Applicants' argue that there is no need in the claimed invention to isolate Formula IV or V. This argument is not persuasive as for some claims, such as claim 1, isolation is not an excluded claim limitation. For the claims that exclude isolation, it is well within the expected skill of the practitioner to operate a process continuously.

Applicants' discusses the wastefulness of the process of WO 96/33980, however, this reference was not applied against applicant.

Applicants' argue that there is no disclosure in the prior art references that the Formula's IV and V can be taken from their preparation and introduced into the next step in a solution of an organic solvent. Again, this argument is not persuasive as it is well within the expected skill of the practitioner to operate a process continuously.

Therefore, the 35 USC 103(a) rejection is maintained for claims 1 and 4-8 and is also applied to new claims 30-52.

In regards to the requirement to exclude isolation steps in some claims, it is noted that it is well within the expected skill of the practitioner to operate a process continuously. In regards to step (a) in the new claims, it is noted that the prior art reference WO 02100649 discloses the use of a water soluble inorganic reducing agent sodium hydrosulfite which is another name for sodium dithionite. Also, WO 02100649 discloses extraction with an organic solvent of methylene chloride. WO 02100649 also discloses the polar protic solvent of water. While some of Applicants' claims include tert-amyl alcohol as the polar protic solvent in steps (a), (b) and (c), it is noted that the prior art references all disclose polar protic solvents, in particular, water, methanol and formic acid. However, the Courts have decided per In re Boesch, 205 USPQ 215 (1980), that the optimization of variables in a known process is prima facie obvious. Therefore, the claimed process would have been suggested to one skilled in the art. While JP'515 discloses calcium carbonate as the alkali metal base, it is again noted that optimization of variables in a known process is prima facie obvious.

Claim Objections

Claims 45 and 51 are objected to because of the following informalities: Specifically, claim 45 does not end in a period. Claim 51 has a typographical error in step (c), specifically, "Formula H" should be "Formula II". Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

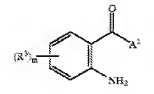
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4-8 and 30-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,294,532 in combination with JP 11228515 (English Translation attached) and WO 02/00649.

Determining the scope and contents of the prior art

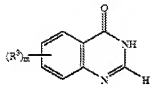
US Patent NO. 6,294,532 discloses on column 32, the compound XVII which can prepare XIV (see column 31, line 5 and column 32, line 15):

(XVII)



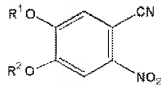
and

(XIV)



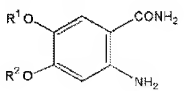
(which corresponds to applicants step (c) and applicants' formulas V and II). When A1 is an amino group, formic acid or an equivalent can be utilized to cause cyclisation to obtain formula XIV, column 32 lines 33-48. An equivalent of formic acid is disclosed as formamide, see line 23, column 32. Preferred values for R3 and m are seen on column 7 wherein m is preferably 1 or 3 and X7 is preferably -O-; on column 10 wherein R3 is preferably R15X7; and on column 11 wherein preferred values of R15 include methyl and 3-morpholinopropyl. The compound XIV is an intermediate to prepare compounds of the formula (I) which are useful for the treatment of specific cancers, column 2.

JP 11228515 discloses the process of preparing (2) from (1):



(1)

and

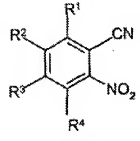


(2)

(which corresponds to applicants steps (a) and (b) and formulas III, IV and V), page 2 of translation. The preparation is useful for preparing anthranilamides useful in the

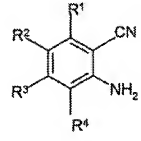
production of medicines (page 1). R1 and R2 can be substituted or unsubstituted alkyl, such as methyl ethyl and propyl, page 3. The process utilizes a palladium catalyst for the hydrogenation and is carried out in the presence of an alkali metal bases such as calcium carbonate in a polar protic solvent such as methanol, page 4.

WO 02/00649 discloses the process of preparing compounds of the formula (IX) with compounds of the formula (XIII), page 59 and 57:



(XIII)

and



(IX)

(which corresponds to applicants step (a)). R2 and R3 can be methoxy or 3-morpholinopropoxy, see page 78 which discloses the use of sodium hydrosulfite as a water-soluble inorganic reducing agent in the preparation of the compound H, see also page 77. Preferences for R2 and R3 are also seen wherein R2 and R3 are X1R9 wherein X1 is oxygen and R9 can be methyl or one of R2 and R3 can be –OC1-5alkylR33 wherein R33 is 3-morpholinopropoxy. The compounds of the formula IX are useful for preparing compounds of the formula (I) which are useful for the treatment of specific cancers, page 3.

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that US Patent No. 6,294,532 discloses the process of preparing (XIV) from (XVII) which corresponds to step (c) of the claimed invention. US Patent No. 6,294,532 does not disclose the compounds of formulas (III) and (IV) as found in the instant claims or the process steps of (a) and (b) as in the instant claims.

The difference between the prior art of JP 11228515 and the instant claims is that JP 11228515, while disclosing a process which corresponds to steps (a) and (b) of the claimed invention, does not disclose the compound of formula (II) nor process step (c).

The difference between the prior art of WO 02/00649 and the instant claims is that WO 02/00649m while disclosing a process which corresponds to step (a) of the claimed invention, does not disclose steps (b) and (c).

Resolving the level of ordinary skill in the pertinent art

However, minus a showing of unobvious results, the claimed process is no more than a selective combination of prior art teachings done in a manner obvious to one of ordinary skill in the art since each step of the process appears to be relatively complete in itself and there is no indication of an interaction between steps of such a type that would lead one of ordinary skill in the art to doubt that a substitution of alternative steps known to the art could be made. In re Mostovych, 144 USPQ 38 (1964). All of the claimed steps (a), (b) and (c) were known in the prior art and one skilled in the art could have combined the steps as claimed by known methods with no change in their

respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday from 6:00am until 2:30pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Anderson/
Primary Examiner, AU 1626

24 November 2008

Rebecca Anderson
Primary Examiner
Art Unit 1626, Group 1620
Technology Center 1600